

**REMARKS**

The Office Action mailed August 25, 2003 (Paper No. 13) has been carefully reviewed and the foregoing amendments are made in response thereto. In view of the amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

At the outset, the undersigned is appreciative for the telephone conference with the Examiner on January 20, 2004, in which the Examiner requested clarification between the term "continuous" as recited in the claims, and the term "pulse" as seen in the prior art. In this regard, claim 1 has been amended above to clarify that a continuous voltage excludes electroporation pulses of short duration in the order of milliseconds. Support for this amendment may be found in the specification at page 2, lines 10-12 and lines 30-31. Applicants respectfully submit that no prohibited new matter has been introduced by the amendment.

***The Rejection of Claims 1-11 Under 35 U.S.C. § 103(a) First Paragraph***

Claims 1-11 remain rejected under 35 U.S.C. § 103(a) for allegedly being unpatentable over U.S. Patent 5,186,800 to Dower. According to the Office Action, even though Dower does not disclose applying a voltage of not more than 50 volts for a period of at least 30 seconds or two minutes continuously, one of skill in the art would be motivated to apply such voltage conditions to avoid denaturation of intracellular material. Further, as the Examiner asserted in the telephone conference on January 20, 2004, a voltage as provided by the pulse duration disclosed in Dower is still continuous over the duration of the pulse.

Applicants believe that the amendment to claim 1 above renders the rejection moot. Claim 1 has been amended to clarify that a "continuous" voltage excludes electroporation pulses of short duration in the order of milliseconds as disclosed in Dower. Indeed, the voltages taught in Dower include pulses of 2 to 20 msec, and more particularly 3 to 10 msec (see col. 8, lines 20-23). Such voltages are excluded by the claims as amended, which exclude millisecond pulses. Moreover, claims 10 and 11 in particular require application of a continuous voltage of at least 30 seconds and at least two minutes, respectively, which is far outside the range disclosed in Dower.

According to the Office Action, one of skill in the art would be motivated to adjust the conditions of Dower to apply a continuous voltage of not more than 50 volts for a period of at least thirty seconds to avoid denaturation of intracellular material. Applicants respectfully disagree. Dower's disclosure relates to electroporation. As disclosed in the present specification, electroporation involves the application of high voltages, typically in excess of 1 kV, in pulses of short duration, typically in the millisecond range (see p. 2, lines 10-16). In fact, as disclosed in Dower at col. 7, lines 27-43, the conditions suggested by Dower provide an electric field strength of at least about 5 kV/cm, usually at least 10 kV/cm, and preferably above 15 kV/cm. As also described in Dower (col. 7, lines 36-38), a pulse generator voltage of 1kV will provide a field strength of 5 kV/cm at the preferred electrode spacing of 2.0 mm. Thus, the preferred field strength (above 15 kV/cm) as taught by Dower involves the application of voltages in excess of 3 kV, which is well above the limit of 50 volts recited in claim 1 of the present application.

Given that Dower sets a lower limit of 5 kV/cm (1 kV), with preferred voltages of 15 kV/cm (3 kV) and higher, Dower teaches away from an optimization involving very low voltages such as those recited in the present claims. In fact, Dower suggests at col. 8, lines 18-19, to use even "higher voltages" with "more recalcitrant cell types." Thus, Dower teaches toward using higher voltages than those specifically disclosed, rather than the very low voltages as recited in the present claims.

According to the Federal Circuit, a prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). A *prima facie* case of obviousness may be rebutted by showing that the art, in any material respect, teaches away from the claimed invention. *In re Geisler*, 116 F.3d 1465, 1471, 43 USPQ2d 1362, 1366 (Fed. Cir. 1997).

Thus, Dower teaches away from the claimed invention by disclosing preferred voltages of at least 1 kV and preferably at least 3 kV, with even higher voltages recommended for "recalcitrant cell types." Further, the millisecond pulses disclosed in Dower are excluded from the definition of continuous voltage as set forth in the present specification, which has now been

included in the claims. In view of the amendments and remarks submitted herein, reconsideration and withdrawal of the rejection are respectfully requested.

***The Rejection of Claims 1-11 Under 35 U.S.C. § 112 Second Paragraph***

Claims 1-11 were rejected under 35 U.S.C. § 112 second paragraph because the term “continuous” is allegedly indefinite. Without acquiescing to the grounds of the rejection and solely to expedite prosecution, Applicants have amended claim 1 to clarify that a continuous voltage excludes electroporation pulses of short duration in the order of milliseconds, as disclosed in the specification. Reconsideration and withdrawal of the rejection is requested.

***Conclusion***

In view of the foregoing amendments and remarks, Applicants respectfully request withdrawal of all outstanding rejections and early notice of allowance to that effect. Should the Examiner believe that a telephonic interview would expedite prosecution and allowance of this application, she is encouraged to contact the undersigned at her convenience.

Applicants believe that no fees are required with this filing, however, except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No.50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully submitted,

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